ORGANIZATION OF PNEUMONIC EXUDATES.

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The purpose of this paper is (*a*) to show how the exudate in the lung alveoli starts to change into connective tissue, and (*b*) to throw light on the relation of organizing pneumonia to acute lobar pneumonia.

The organization into vascular fibrous tissue of intra-alveolar lung exudates, especially as this occurs in wide areas following an acute lobar pneumonia, has been extensively studied. Important contributions have been made by Laennec,[1] Marchand,[17] Cohn,[31] von Kahlden,[32] Herbig,[33] Ribbert,[41] Cornil,[42] Vogel,[43] Delafield,[56] Milne,[74] Kidd,[75] Kline[79] and others.

It has been determined that the intra-alveolar exudate of fibrin, including the exuded cells in its meshes, shrinks and condenses, thus leaving a space between it and the alveolar wall, though retaining contact with the wall by adhesions which may be either extensive or slender and filamentous. These connections between the retracted fibrin plugs and the wall may be formed of fibrin or of elongated cells. The fibrin, when originally deposited, is often continuous from space to space through the pores of Cohn,[31] which establish fine connections between adjacent air spaces belonging to different infundibula, and, when general retraction of the fibrin exudate occurs, these communicating strands stand out very distinctly. Pulmonary epithelium and other exuded cells appear in the gaps between the plugs and space walls, and some of the flattened epithelial cells, which have a spindle form when seen on edge, are often applied to the plug surface. About two weeks after the onset of the pneumonia, cells with elongated nuclei, exhibiting all transitions to fibroblasts, appear within the substance of the fibrin plugs and on their surface. At this time, or a little later, capillary vessels given off from the capillaries of the space walls enter the plugs by traversing the above-described adhesions between the space wall and plug. This process and also the communicating bands which traverse Cohn's pores, and later are changed into connective tissue, have been demonstrated beyond doubt by means of serial sections by MacCallum[60] and others. As time passes the fibrin is more or less completely absorbed and replaced by fibrillated connective tissue, and then the appearance of two networks is produced in sections, one the alveolar walls and the other the organized intercommunicating exudate. The alveolar walls also show varying degrees of fibrous thickening which may reach the point of obliterating the gaps between them and the fibrin plugs, so that the distinction between organized exudate and basic lung structure, that is between the two networks, is completely lost and the whole tissue changed into a dense connective-tissue mass, devoid of spaces, tough and airless.

There has been much discussion about the origin of the connective tissue in the plugs, some observers thinking it an ingrowth either from the pleura and interlobular septa (Eppinger,[11] Cohn[31]), or from the bronchiole walls (Ribbert,[41] Herbig[33]), or from the walls of the air spaces (von Kahlden[32]). Others have thought that fibrogenic cells migrated into the plugs (Aufrecht,[40] Cornil[42]), or that a late secondary exudation of fibroblasts occurred not evoked by the original bacterial irritant (Ziegler,[65] Josephson[24]), or that cells originally exuded changed into fibroblasts (Marchand[17]). Still others have believed that the pulmonary epithelium surrounded and entered the plugs and became connective-tissue cells (Woronochin,[8] Lindermann[26]), but this view has never been generally accepted. Perhaps the strongest current of recent opinion sets toward the derivation of the connective tissue, along with the vessels, from the wall of the air space in which each plug lies, though extensions of connective tissue into the plugs from pleura, interlobular septa and bronchiole walls, confirmed by various observers, are regarded as established but exceptional phenomena.

Organization of intra-alveolar exudates, as described, has been observed in bronchopneumonia, in tuberculous consolidation and about infarcts and abscesses (Frankel[36]), but its most extensive development, and that which has attracted the most attention, is as a sequel of lobar pneumonia. Here the lesion is seldom co-extensive with the original pneumonic exudate, but involves portions only of the lung originally inflamed.

The question whether the lobar pneumonias which go on to organization are a separate type of lesion from the outset or whether appropriate causes may effect this change in any lobar pneumonia is still undecided. Those who hold the latter view name as causes debility (Heschl,[5] Milne[74]), alcoholism (Marchand[17]), presence of excess of fibrin (von Kahlden[32]), excessive sluggishness of the lymph circulation (Köster[19]), insufficient pus cells in the exudate to effect its absorption (Flexner[54]), and the presence of an excess of serum (Kline[79]).

My contribution is based on the study of two sets of material—namely, (*a*) 603 lung sections, practically all showing pathologic changes of some kind, obtained from 249 cases whose autopsies I either did or attended. In many of these cases I studied the patients during life, and in all of them there are full clinical, autopsy and microscopic records; (*b*) 153 lung sections given me by Dr. Delafield, obtained by him at autopsy, all showing some lesion. In only a few of these, however, are clinical and pathologic records available.

Before analyzing the observations on this material it is necessary to define what an intra-alveolar connective-tissue plug is and to discuss briefly some general characters of pneumonic exudates.

A typical connective-tissue plug of fairly recent origin, perhaps two or three weeks old, is composed of a dense, refractive substance taking a strong eosin stain. It is of a finely granular structure and may also show a distinct fibrin reticulum, either compact or, in places, more open (Fig. 1). The plug does not fill the alveolus in which it lies but regularly leaves a residual space which may be empty, or may contain polynuclear, mononuclear, blood or epithelial cells. Some flattened epithelial cells are often applied to the plug surface and have a spindle form when seen on edge. In sections a plug may appear to lie free in the alveolus, or it may be connected in part to the alveolar wall, either through broad areas of contact or by slender strands or bridges of fibrin or of cells. Tenuous strands may also extend through mural pores and so connect the plug to

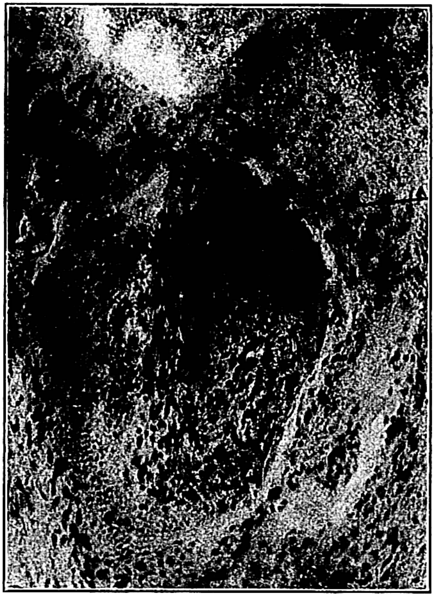

Fig. 1.—Organizing pneumonia, death on the twentieth day. Typical organizing fibrin plug adherent to the alveolar wall at *A*, but leaving a residual space elsewhere. Elongated fibroblast nuclei may be seen in the plug. × 263.

plugs in neighboring spaces (Fig. 2). The dense plug substance often looks incompletely separated into rounded masses by partial fissures. In the plug are regularly included nuclei, some polynuclear and often pyknotic and deformed; others large, vesicular and rounded; and finally oval or distinctly elongated vesicular nuclei which can be seen in all stages of elongation until they appear as fibroblast nuclei with their cell bodies and associated fibrils sharply distinct (Fig. 1). When simply oblong without defined cell body these early fibroblasts do not resemble the epithelial cells applied to the plug surface, but when the long cell bodies appear, and before the characteristic fibrillar ground substance is deposited, I know of no way of distinguishing the early fibroblasts which lie near and parallel to the surface, from the epithelial cells lying against the plug, as above described (Fig. 3). It is evident that in this difficulty lies the origin of the belief of some observers, above referred to, that epithelium may be metamorphosed into connective tissue. Fibroblasts deep in the plug substance, however, and

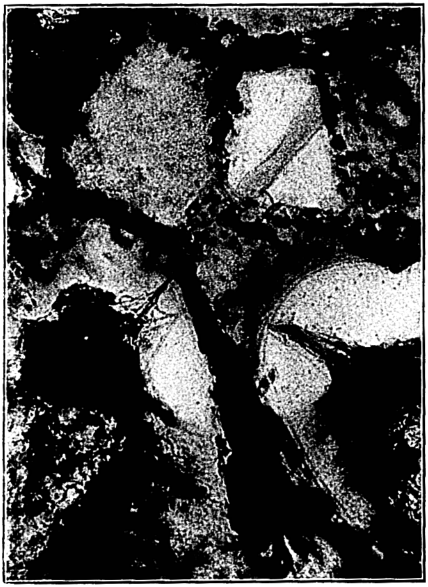

FIG. 2.—Organizing pneumonia. Slender fibrin strand connecting adjacent plugs through a Cohn pore. × 213.

penetrating it in different directions, may, I believe, be safely identified as such.

I have gained the impression that pyknotic and deformed nuclei are more numerous in early plugs, twelve days or so old, than in late ones, three or four weeks old, and that some of the cells in the plugs, especially the polynuclears, are destroyed and disappear, while some of the mononuclears go on to develop into fibroblasts (Fig. 4).

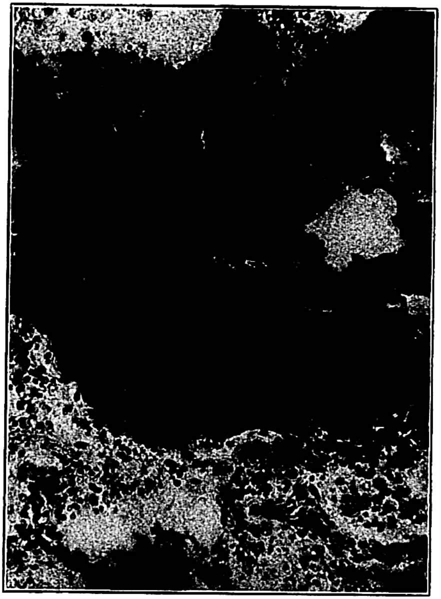

FIG. 3.—Organizing pneumonia death on the twentieth day. Spindle-shaped cells along the plug edges, some separate and some adherent; impossible to say which are epithelium and which fibroblasts. × 213.

Bloodvessels budding from mural capillaries unquestionably penetrate these plugs, but I am convinced that they do not penetrate them all or even a majority of them in the early stages, that is, not until after four or five weeks.

When occurring in any number, the dark red anastomosing plugs with elongated nuclei and fibroblasts are strikingly evident at the first low-power glance (Fig. 5), but in order to determine whether there is definite evidence that the exudate in a particular alveolus promises to organize and so shall be considered an early connective-tissue plug, certain criteria must be set up. It is evident that the amount of retraction and of condensation of the fibrin is not a significant feature and will be the less developed the earlier the stage of the process. It is also evident that the same will be true of the ingrowing capillaries.

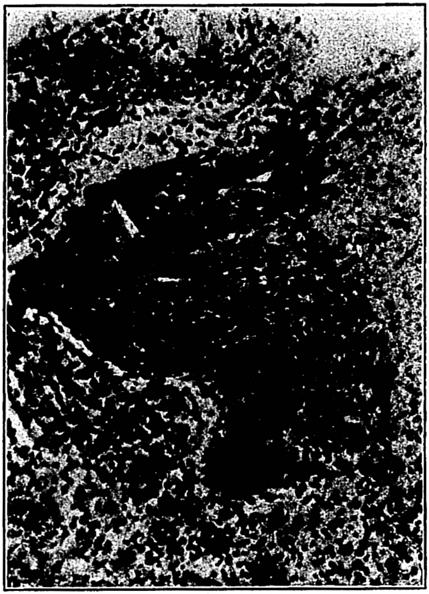

FIG. 4.—Pneumonia secondary to bronchoesophageal fistula. Fibrin plug with some elongated nuclei and many pyknotic polynuclear nuclei. × 213.

Every alveolus which contains reticulated fibrin or a dense granular mass of exudate with a strong affinity for eosin and elongated vesicular nuclei in the fibrin mass, exclusive of those which may be confused with epithelium as above described, promises organization of its exudate, and has been considered to contain an early connective-tissue plug in the present study.

In order to justify this statement it is necessary to consider certain components of pneumonic exudates.

Fibrin varies greatly in quantity. Only rarely does it occupy as much or more space than the cellular elements as a whole. It may be totally absent, so far as this can be established, through the absence of any demonstrable strands, fibrillæ or reticulum in the spaces. It not infrequently is very unevenly distributed, occurring in large and even overwhelming quantity in a few spaces and scarcely recognizable in most of the rest. Moreover, it is frequently asymmetrically deposited in individual spaces, forming a dense reticulum on one side and fraying out to fine isolated fibrils in the opposite portion (Fig. 4). Such asymmetrical concentrations apparently often form the basis of connective-tissue plugs. In many sections I have observed such concentrations along the pleural boundaries, the fibrin being regularly denser on the side next the supporting tissue (Fig. 6). The same observation has been made by Cornil.[42] I can suggest no reason unless these portions of the alveoli move less with respiration, and so the fibrin is less stretched and less insufflated by the tidal air during its deposition. The subsequent

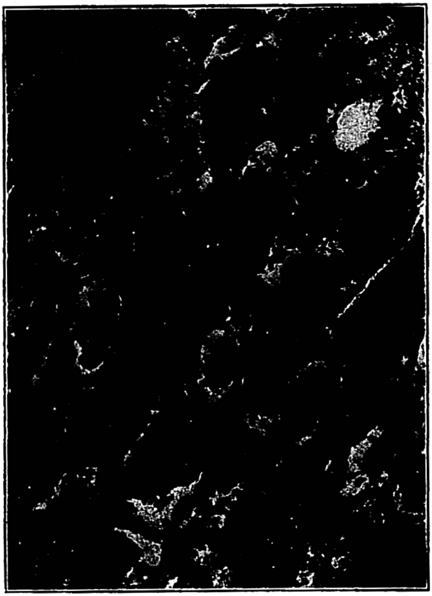

Fig. 5.—Organizing pneumonia, death on the twentieth day. Typical organizing intra-alveolar plugs with some thickening of the alveolar walls. × 63.

formation of plugs in such regions, to the exclusion of others, perhaps explains the view advanced by some observers that the connective tissue of the plugs is derived from pleural and trabecular connective tissue. At any rate the fibrin is usually unequally distributed, a lot in some spaces, very little in others and often asymmetrically deposited in individual spaces, so that a partial absorption of the exudate would result in leaving fibrin plugs only partly filling the spaces, a probable factor in plug-production as well as subsequent shrinkage and condensation. It is not at all unusual to see sections, especially of pneumonias dying within two weeks of their onset, with a large number of typical dense red staining fibrin plugs which show no elongated nuclei (Fig. 7). Whether these represent the earliest stage of connective-tissue plug formation, and whether fibroblasts would subsequently have appeared in them had life been prolonged, as Delafield[56] thought, I have no way of knowing. At any rate they are excluded by the above definition from the plugs with indications of organization. There is no obvious reason why they cannot be absorbed as well as any other fibrin exudate.

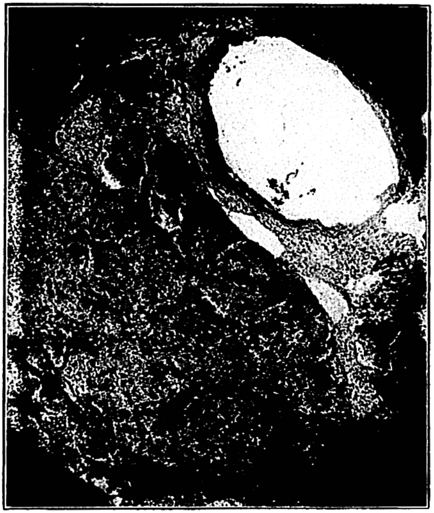

FIG. 6.—Lobar pneumonia, death on the eighth day. Fibrin concentrated in alveoli along a large vessel and mostly on the side of the spaces next the vessel sheath. × 40.

Serum is coagulated in various forms by hardening agents and appears in lung sections as fine granular matter, as a foam work or as a homogeneous coagulum enclosing cells and some round lacunæ, presumably air bubbles. When in the latter form it may stain very faintly or very strongly with eosin, apparently depending on how much blood pigment it held in solution when coagulated. Kline,[79] as a result of experiments on dogs, inclines to the belief that serum is an essential factor in the production of organizing pneumonia; but I have never seen long vesicular nuclei or fibroblasts in even the deepest staining serum coagula in lobar pneumonia, and almost never in sections of other lesions. One most striking alveolus from an organizing pneumonia contained a homogeneous serum coagulum, in the central part of which was included a distinct wisp of fibrin fibrillæ. In the serum were several cells with round vesicular nuclei but none elongated, while those in the fibrin were definitely elongated and of the early fibroblast type

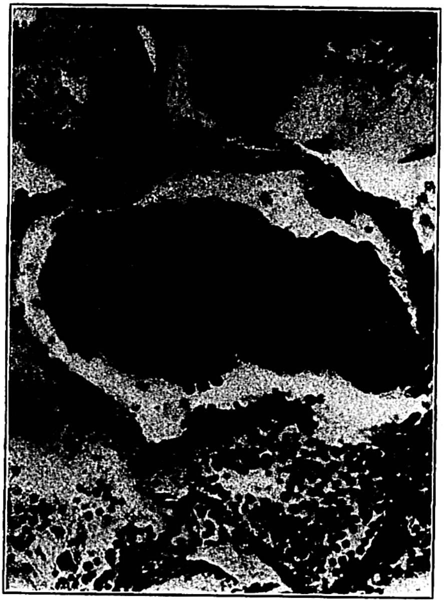

FIG. 7.—Lobar pneumonia. Fibrin plug without fibroblast nuclei. × 213.

(Fig. 8). I can see no reason for believing that exuded serum favors the development of fibroblasts as exuded fibrin does.

The relations of the exuded cells to the connective-tissue plugs are various. Red blood cells are often included in the plugs, but in no section did fibroblasts appear in alveoli filled with blood alone even when it had probably been there for some time.

Polynuclears are, of course, entangled in the reticular fibrin or included in the dense plugs, often in large numbers; but they seem to exert no influence on organization. In fact, as above mentioned, they undergo degeneration with pyknosis of their nuclei (Fig. 4), mostly before the end of the second week from the onset in lobar pneumonia, so that after that time few are seen in the plugs.

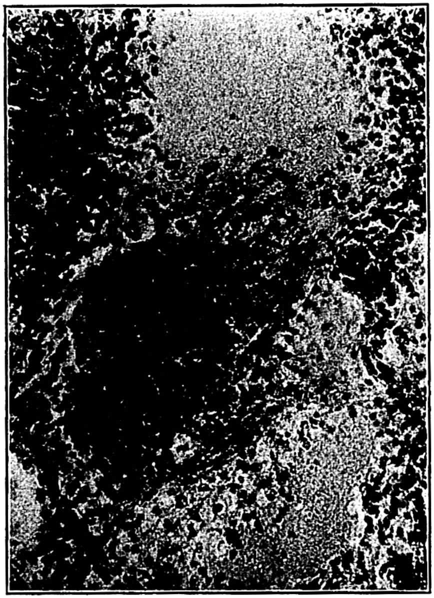

FIG. 8.—Organizing pneumonia, death on the thirteenth day. Large alveolus filled with coagulated serum, with a mass of fibrin in the center. The nuclei in the serum are round; some of those in the fibrin are distinctly elongated. × 213.

The epithelium is often seen applied to the plug surface, as above mentioned (Fig. 3), whether as a result of simple desquamation from the space wall or by a true investing proliferation, as has been thought by some observers, it is difficult to be sure. The difficulty of distinguishing such cells from fibroblasts has already been explained. Sometimes definite dense retracted plugs with typical long vesicular nuclei occur where no reticulated fibrin can be demonstrated in any of the alveoli in the section, but where there is much desquamated epithelium, and all stages can be traced from loose, discrete, desquamated epithelial cells in some alveoli to their conglomeration into dense plugs in others, in some of which elongated nuclei occur (Fig. 9). Thus the formation of organizing plugs out of epithelium instead of fibrin apparently occurs, though rarely. Of course, some fibrin-binding substance may be present in such cases without presenting the usual reticulated appearance.

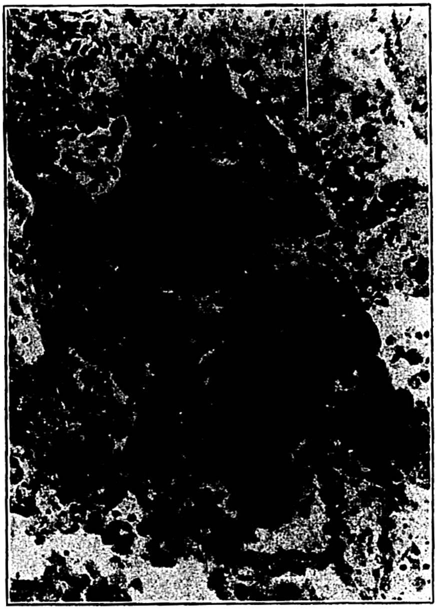

FIG. 9.—Secondary bronchopneumonia in an adult. Much epithelium in the alveoli, in one case concentrating to form a plug. Fully formed plugs with elongated nuclei and traces of their epithelial composition still distinguishable occur in the same section. × 213.

As already stated the fibroblasts are derived from cells with a single rather large vesicular nucleus. Much has been written about such cells in inflammatory processes, and I have no new light to throw on their origin. They presumably belong to the mesenchyme group, and I believe they exist in the intra-alveolar exudate from the start rather than that they represent a secondary migration induced by a new stimulus, because they lie deep in the dense fibrin plugs when they first take on the oblong shape. Mononuclear cells occur in most intra-alveolar exudates—some have no visible cell body and a small dense nucleus, the lymphocyte or round-cell type; some have a larger vesicular nucleus and an appreciable cell body, the endothelial type, and may be hard to distinguish from pulmonary epithelium. How many kinds of cells the mononuclears represent, from how many sources of origin, whether they arrive through the blood or lymph channels, what their various functions and destinies may be, is still somewhat uncertain. That one group of them may become fibroblasts, however, is generally accepted. The only new ideas I have to offer about them in organizing pneumonias is that they exist in the exudate from the start (a suggestion made long ago by Marchand[17]), that the presence of fibrin in some way favors their change into fibroblasts and that this change is not dependent on the ingrowth of buds from mural capillaries because fibroblasts regularly begin to develop before any vessels appear and may often attain full development where no vessels can be demonstrated. If the fibroblasts were derived from the mural connective tissue by ingrowth, as the vessels are from the mural capillaries, it should be easy in early stages to see spots in the plugs from which the connective tissue radiated, an appearance I have not seen, instead of a simultaneous change in shape of nuclei scattered all through the plug, which is the usual appearance.

Just as fibrin plugs may be present in many spaces without the presence of any elongated vesicular nuclei, so cells with such nuclei and even definite fibroblasts may occur in the alveoli, without any fibrin and without any plug formation; but I have not met this condition in lobar pneumonia or secondary patchy pneumonia, though in tuberculous lungs it is not very rare (Fig. 10).

The new bloodvessels, about which so much has been written and the manner of whose ingrowth has been demonstrated beyond question in serial sections by MacCallum[60] and others, have not proved as universal as I expected. In fact, not only have they been absent from entire sections showing early plugs with definite early fibroblasts, but quite difficult to find in some lesions of long standing, notably in a case of four and a half months' duration.

Conservatism must be exercised in interpreting vessels as newly formed and pathologic, for the vessels in the normal partitions which partially separate the alveoli springing from the same infundibulum often appear to penetrate or jut into the plugs just as they do in any exudate that occupies the alveoli (Fig. 5).

On the other hand, small thin-walled single vessels cut in cross-section, or short and isolated oblique slices lying in the central portion of the plugs, are definitely newly formed and inflammatory (Fig. 11). This opinion that new-formed vessels in the plugs are not essential and, in many cases, not even a frequent feature of the lesion under discussion, is based not only on the study of ordinary hematoxylin-eosin preparations but also from the careful examination of a number of sections of organizing pneumonias among the slides received from Dr. Delafield, in which he injected the pulmonary vessels with a gelatin Prussian-blue mass, in which the capillary ramifications may be accurately traced.

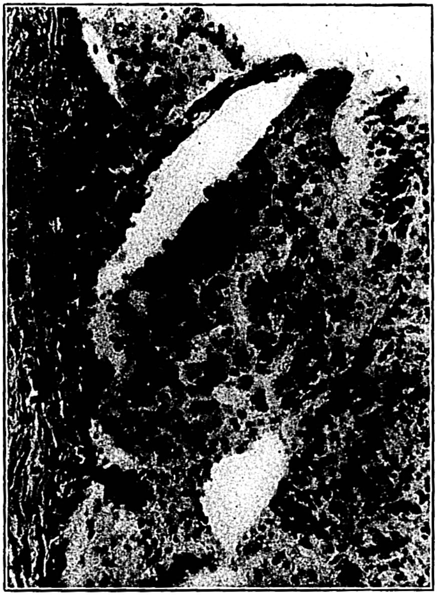

FIG. 10.—Subacute phthisis. Fibroblasts growing in an alveolus with no fibrin and no condensation of the cellular exudate into a plug. × 213.

Connective-tissue plugs, as above defined, are by no means rare in the material studied. They appear in 129 out of my 603 sections and in 48 out of the 153 made by Dr. Delafield, that is, in 23.4 per cent, or over one-fifth of all sections examined.

The term organizing pneumonia has been applied to cases in which the organizing intra-alveolar plugs are numerous, the lesion of lobar distribution and not tuberculous in origin, especially if the patient first falls sick as a lobar pneumonia. Nine of my cases fall in this group, and it is from them that the sections diagnosed as organizing pneumonia were taken. A study of the records of these cases does not support the view of some observers that old age and debility are important etiologic factors. Thus the average age is forty years, the youngest twenty, the oldest seventy-two, and only 1, the last mentioned, over sixty. The nutrition and previous general health, as far as it can be determined from the records, was fair or good in all but 2. Excessive use of alcohol is only reported in 1 case. Seven out of 9 of my series were males. The onset was sudden and identical with that of ordinary lobar pneumonia in 6, but of a more gradual character in 3, the most indefinite being in the old man of seventy-four years, who was, however, feeble-minded and unable to give a reliable account of himself, and of

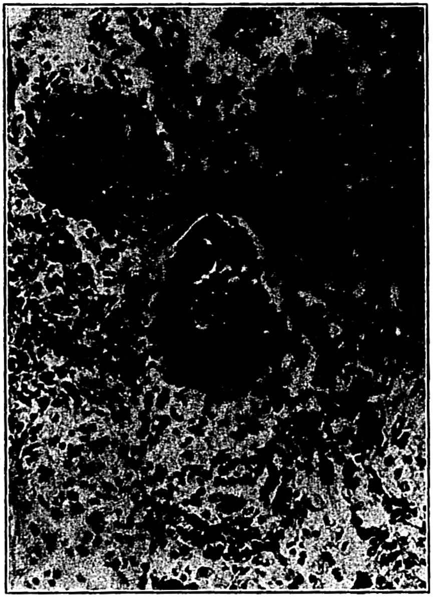

Fig. 11.—Pneumonia secondary to bronchoesophageal fistula. New-formed vessels in an organizing fibrin plug. × 213.

the other 2, one in a man, very sick, who was taken ill three months before admission, where recollection of the type of onset could well have been confused.

There is nothing significant about the location of the consolidation, as is evident from the following table:

Entire right lung, 3.
Entire left lung, 2.
Entire left and part of right lung, 1.
Right upper and middle lobes, 1.
Both lower lobe, 1.
Right upper lobe, 1.
Left lower lobe, 1.

In 6 cases there were fibrous pleural adhesions; in 2 cases a fibrin exudate. The duration varied from eight to one hundred and thirty-five days. The average from 8 cases being forty days. Other lesions of lung and pleura were frequently present. Abscesses or cavities or both occurring in 5 cases and a double empyema in a sixth one. The microörganism was only determined in 2 cases: 1 a pneumococcus type I and the other a pneumococcus type II.

The intra-alveolar plugs themselves present different stages in the process already described in detail. As has been above indicated new vessels in them are not frequent, being notably hard to find in the case of a hundred and thirty-five days' duration, and only found in 3 others of the series, 1 of uncertain duration and the other 2 of thirteen and thirty-five days respectively.

This series of 9 organizing pneumonias is very similar in general to other series that have been reported, though the case of eight days' duration is a very early one. Cavities, abscesses and pleural adhesions have been many times observed as concomitant lesions. I have given this recapitulation of my cases not to illustrate any new features, but rather to show that my observations are based on true cases of organizing pneumonia similar to those reported by other observers.

It is evident not only from my small series but from the literature that organizing lobar pneumonia is not a rare lesion at autopsy. On the other hand a healed lesion corresponding to it, that is a lobe extensively changed into connective tissue, is a decided rarity. Such cases when found may be impossible to distinguish from cases which have started as bronchopneumonias or from cases primarily pleurogenic. I have seen but one such case in an adult with extensive fibrosis of the lung tissue and multiple large bronchiectasiæ involving the right upper and middle and the left lower lobes in a woman, aged forty-eight years, without any history of previous lung trouble.

The deduction from all this is that organizing lobar pneumonia, once fully established, proves fatal in the vast majority of cases.

Organization of the intra-alveolar exudate, however, is not at all confined to sections from cases in which the lesion is pronounced enough to be called organizing pneumonia, as shown by the following list of the anatomic diagnoses of the sections in my own series which show organizing plugs:

Organizing pneumonia	31
Lobar pneumonia	38
Bronchopneumonia	5
Secondary or patchy pneumonia	5
Tuberculosis pneumonia (all forms)	27
Interstitial pneumonia	6
Infarcts	5
Lymphatic leukemia	3
Congestion and edema	3
Pneumonia secondary to bronchoesophageal fistula	1
Chronic congestion with heart disease	1
Cancer	2
Compressed lung beneath empyema	1

The incidence of organizing plugs in the ordinary forms of consolidation is shown in the following table, again from my own series:

	Total number of sections exhibiting this lesion.	Number of sections of this lesion which. show organizing plugs	Sections of this lesion showing organizing plugs. Per cent.
Lobar pneumonia	101	38	37.6
Bronchopneumonia	55	5	9.0
Secondary or patchy pneumonia	59	5	8.4
Tuberculous pneumonia (all forms)	87	27	31.3

Organizing plugs are most frequent in lobar pneumonia, and here also the fibrin plugs without early fibroblasts are most often seen. Of 16 sections in which fibrin plugs without fibroblasts occur, 9 are in sections of lobar pneumonia. In lobar pneumonia dense fibrin, one of the components of organizing plugs, is present in some alveoli in nearly half the sections, and in many such specimens some elongated cells appear in the fibrin. There is thus more or less incipient organization of the exudate in over one-third of all lobar specimens examined, but the lesion does not reach sufficient development or extent to warrant calling it organizing pneumonia. In other words the sections of lobar pneumonia and of organizing pneumonia, taken together, apparently represent a series exhibiting various degrees of organization from none up to the extensive examples, and the line of definition between lobar pneumonia and organizing pneumonia becomes an arbitrary one. Numerically stated, of 134 sections of lobar consolidation 54 show no tendency to organization, though fibrin and mononuclear cells regularly occur in the exudate; 9 show distinct dense fibrin plugs but no elongated nuclei; 38 show organizing plugs but not in sufficient numbers to be called organizing pneumonia; while 33 must be considered frank organizing pneumonia.

The proportionate figures hold also in general for the cases from which these sections were taken: of 48 cases of lobar pneumonia, 24 showing no organization, 15 showing minor amounts of organization and 9 being classed as organizing pneumonia.

On this basis I believe that organizing pneumonia, or the "lobar pneumonia with connective tissue" of Delafield, is not a separate lesion or disease but rather a variety of lobar pneumonia, the extreme expression of a tendency that exists in many cases of lobar pneumonia.

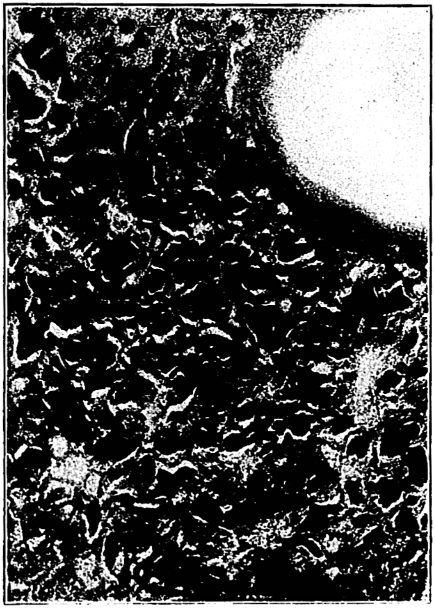

FIG. 12.—Persistent bronchopneumonia in an adult. Many organizing plugs in alveoli near an inflamed bronchus. × 35.

In bronchopneumonia organization of the exudate in the bronchial wall is, of course, very frequent, but the formation of the connective-tissue plugs here under discussion is comparatively uncommon—5 times in 55 sections in my series. Age may be a factor, though typical plugs are present in sections from an infant under one year. In the Delafield sections there are several from persistent bronchopneumonias in adults in which organizing fibrin plugs form a prominent feature of the lesion (Fig. 12).

In the secondary patchy consolidations which occur as terminal lesions in many conditions, especially in adults, intra-alveolar organization is again comparatively uncommon, 5 sections out of 59 in my series. In these cases there is in general more serum and red cells and less fibrin, but how much this composition of the exudate has to do with a relatively smaller number of plugs, I do not know.

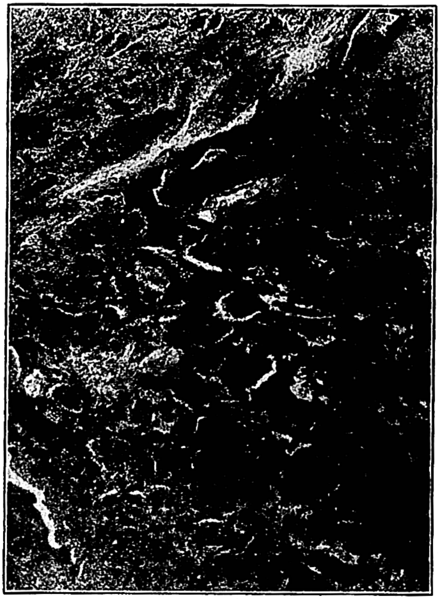

Fig. 13.—Tuberculous pneumonia. Organizing plugs in many spaces. × 35.

In tuberculous inflammations of the lung, on the other hand, a large proportion of the specimens, 27 out of 87, show organizing fibrin plugs, and in some cases of phthisis the lesion seems to be based on the development of connective-tissue plugs in nearly every alveolus, necrosis of this exudate subsequently occurring over areas of varying extent (Fig. 13). Here mononuclear cells are often predominant in the exudate, and instances in which they are changing into fibroblasts in spaces in which no fibrin and no plug substance are present are not very unusual. In lobar pneumonia the dense fibrin plugs are common and the fibroblasts comparatively rare; in tuberculous pneumonia, on the contrary, I have found the fibroblasts numerous, even developing when there is no fibrin, and when fibrin is exuded, fibroblast nuclei readily develop in it.

Organization of the pneumonic exudate has generally been regarded as beginning about the fourteenth day after the onset of the symptoms, perhaps because it was thought that the new connective tissue was derived from the alveolar wall along with the budding capillaries which are first demonstrable at about this date. Cornil,[42] however, describes elongated fibrogenic nuclei on the seventh day in human pneumonia, and on the sixth day in experimental pneumonia in dogs. My belief that the fibroblasts develop from cells contained in the original exudate, especially in the presence of fibrin, but antecedent to and quite independent of the vascularization of the plugs, is confirmed by finding elongated vesicular nuclei in fibrin plugs in 2 cases of lobar pneumonia dying

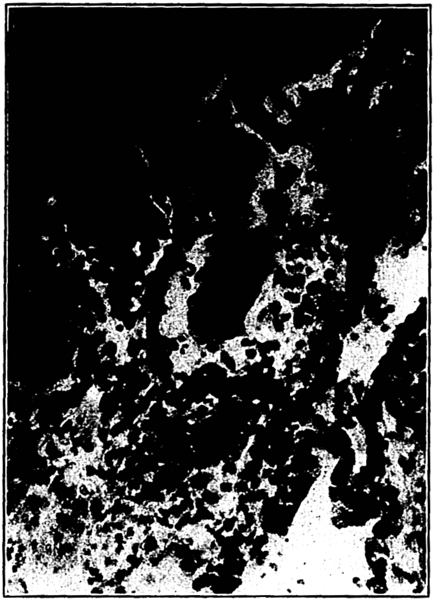

FIG. 14.—Lobar pneumonia, death on the fifth day. Fibrin plug with elongated nuclei. × 263.

on the fifth day (Fig. 14) and in 2 other cases dying on the sixth day, and also 1 case, classed as organizing pneumonia, dying on the eighth day.

There is an obvious objection to the ideas here presented, namely, the fact that, clinically, cases of organizing pneumonia are decidedly unusual while complete resolution occurs in the vast majority of the lobar pneumonias that recover. Moreover, in those of my cases which died, where the duration of the disease was known, the average day of death in those with no organization or with plugs in which the nuclei are not typically elongated, was the eighth day, while in those with organizing plugs it was the ninth day—not a significant difference. There is no evidence, however, and no reason to suppose that the presence of oblong or oval nuclei in a plug of intra-alveolar fibrin interferes in any way with its complete solution, or that the condition which exists in a lobar pneumonia when it contains many such plugs is any more resistant to resolution up until about the fourteenth day than the cases with no indications of organization. After the cells have fairly become fibroblasts, on the other hand, and especially after the deposition of fibrillar ground substance, usually somewhere between the fourteenth day and the twenty-first day, resolution must become progressively more difficult in that part of the consolidation where such organization is proceeding.

Another objection to the theory here presented is that organization of a few intra-alveolar plugs would seem not unlikely in many cases of lobar pneumonia, for there are numerous cases in which some signs and some roentgen-ray shadows persist after three weeks, to clear up gradually but completely later on, and in such lungs there ought to be left some traces of the process. It is, however, well established, on the other hand, that resolution may be delayed and sluggish without any organization of the exudate or without its development to the true fibroblast stage, and, on the other hand, a few scattered alveoli changed into connective tissue would be hard to find and practically impossible to identify years later when they would simulate an interlobular septum or vascular sheath.

On many points I can offer no light: Why incipient organization is regularly snuffed out by resolution, but sometimes goes on to the full development of a permanent fatal lesion? What makes the exudate contract into plugs? Why fibrin favors the growth of fibroblasts? What are the origin, function and destiny of the various mononuclear cells in pneumonic exudates? How the fibrogenic cells may be identified? and many others.

I believe, then, that pneumonic exudates organize by the metamorphosis into fibroblasts of cells originally exuded and that this change is favored by the presence of fibrin. I further believe that organizing pneumonia is the extreme development of a process which begins in a great many lobar pneumonias and is thus a sequel or complication of lobar pneumonia rather than a separate pathologic process.

BIBLIOGRAPHY.

1. Laennec: Traité d'Auscult. Med., 1819, 1st ed., **1**, 169.
2. Andral: Traité d'Auscult. Med., 1837, 4th ed.
3. Stokes, W.: A Treatise on the Diagnosis and Treatment of Diseases of the Chest, 1837.
4. von Rokitansky: Lehrb. der path. Anat., 1855, **3**, 96.
5. Heschl: Präger Vierteljahrschrift, 1856, **51**, 1.
6. Lebert: Traité d'Anat. Path., 1857, **1**, 648.
7. Foerster: Handbuch d. path. Anat., 1865, **2**, 154.
8. Woronochin: Sitzungsberichte der klin. Akad. z. Wien, 1868, No. 1, **57**, 958.
9. Thierfelder u. Ackerman: Deutsch. Arch. f. klin. Med., 1872, **10**, 209.
10. Buhl: Briefe Lungentz. Tuberk. u. Schwindsucht, München, 1872.
11. Eppinger: Präger Vierteljahrschrift, 1875, **115**, 15.
12. Orth: Comp. d. path. anat. diagnostik, 1876, p. 136.
13. Charcot: Rev. mens. de méd. et de chir., 1878, **2**, 776.
14. Balzer: Rev. mens. de méd. et de chir., 1878, **2**, 776.
15. Coupland: Tr. London Path. Soc., 1879, **30**, 224.
16. Leyden: Berl. med. Wchnschr., 1879, **9**, 201.
17. Marchand: Virchows Arch., 1880, **82**, 317.
18. Marchiafava: Bull. d. r. Acad. Med. di Roma, 1882.
19. Koster: Berl. klin. Wchnschr., 1883, **20**, 748.
20. Feustell: I. D. Braunschweig, 1883.
21. Amburger: Deutsch. Arch. f. klin. Med., 1883, **33**, 508.
22. Wagner: Deutsch. Arch. f. klin. Med., 1883, **23**, 508.
23. Heitler: Wien. med. Wchnschr., 1884, Nos. 50-52.
24. Josephson: I. D. Marburg, 1884.
25. Hanau: Deutsch. Ztschr. f. klin. Med., 1887, **12**, 1.
26. Lindemann: I. D. Strassburg, 1888.
27. Cox: Ziegler's Beiträge, 1889, **5**, 401.
28. Kidd: Lancet, 1890, **1**, 740.
29. Rieder: Jahrb. der Hamburg. Staats-Krankenanstalten, 1890, **1**, 60.
30. Berlin: I. D. Kiel, 1891.
31. Cohn: München. med. Wchnschr., 1893, **11**, 43.
32. von Kahlden: Ziegler's Beiträge, 1893, **13**, 278.
33. Herbig: Virchows Arch., 1894, **136**, 316.
34. Clark: Fibroid Diseases of the Lungs, London, 1894.
35. Aldinger: München. med. Wchnschr., 1894, **12**, 471.
36. Fränkel, A.: Deutsch. med. Wchnschr., 1895, **21**, 153, 177, 190.
37. Borrmann: I. D. Gottingen, 1896.
38. Cornil and Marié: Arch. de méd. exper., 1897, **19**, 185.
39. von Kahlden: Zentralbl. f. allg. path. anat., 1897, **8**, 561.
40. Aufrecht: Lungenentzundungen. spec. Path. u. Ther., Nothnagel, 1899, No. 2, Pt. 2, vol. **14**.
41. Ribbert: Virchows Arch., 1899, **156**, 164.
42. Cornil, V.: XIII Congr. Internat. de méd., Sect. Anat. Path., 1900.
43. Vogel: Ziegler's Beiträge, 1900, **28**, 179.
44. Cacioppo, F.: Clin. med. Ital., 1901, **40**, 47.
45. Lafforgue, E.: Méd. mod., Paris, 1901, **12**, 121.
46. Montel, E.: De la résolution lente de la pneu. lobaire aigue, Paris, 1901.
47. Raybaud, A.: Marseilles méd., 1902, **39**, 193.
48. Nikolskij, J. N.: Dietsk. Med., Moskow, 1902, **7**, 26.
49. Fränkel: Deutsch. Arch. f. klin. Med., 1902, **73**, 484.
50. MacCallum: Ziegler's Beiträge, 1902, **31**, 440.
51. Williamson, O. K., and Emanuel, J. G.: Lancet, 1903, **2**, 814.
52. Révész, V.: Orvosi hetil., Budapest, 1903, **47**, 535.
53. Kohn, H.: Berl. Klinik, 1903, **155**, 1.
54. Dionisi, A.: Arch. de biol., Firenze, 1903, **57**, 711.
55. Flexner: Tr. Assn. Am. Phys., 1903, **18**, 1359.
56. Delafield, F.: Lectures on the Practice of Medicine with Cases, 1903, Part II, p. 221.
57. Hart: Deutsch. Arch. f. klin. Med., 1903-1904, **89**, 108.
58. Bernheim, S.: Méd. orient., Paris, 1904, **8**, 1.
59. Iknayan, N. C.: Illinois Med. Jour., 1904, **6**, 158.

60. Ghedini, G.: Gior d. r. Acad. di Med. di Torino, 1904, **10**, 4s, 442.
61. Ghedini, M.: Arch. di biol., Firenze, 1904, **58**, 1065.
62. Scagliosi, M.: Arch. di anat. path., Palermo, 1905, **1**, 394.
63. Pic: Lyon méd., 1906, **107**, 106.
64. Mylks, W. M.: Queen's Med. Quart., 1906–1907, **11**, 159.
65. Ziegler: Handbuch der spec. Path., 1907, p. 786.
66. Klopstock, F.: Virchows Arch., 1908, **19**, 254.
67. Ducatillon, L. C.: De la splenopneumonie à forme prolongée, Lille, 1908.
68. Allen, R. W.: Lancet, 1909, **2**, 781.
69. Lamar, R. V., and Meltzer, S. J.: Prac. Soc. Exp. Biol. and Med., 1909–1910, **7**, 102.
70. Chatard, J. A.: Johns Hopkins Hosp. Rep., 1910, **15**, 55.
71. McCrae, T.: Johns Hopkins Hosp. Rep., 1910, **15**, 277.
72. McLeod, J. C.: Alabama Med. Jour., 1911, **24**, 309.
73. Bret, J., and Busey: Bull. et mém. soc. méd. des hôp. de Lyon, 1911, **10**, 553.
74. Milne, L. S.: Am. Jour. Med. Sc., 1911, **142**, 408.
75. Kidd, P.: Lancet, 1912, **1**, 1589, 1665, 1746.
76. Caussade, G., and Logre, B.: Bull. et mém. soc. méd. des hôp. de Paris, 1913, 3 s., **35**, 697.
77. Newall, J.: Canada Lancet, 1913–1914, **47**, 12.
78. Gwyn, N. B.: Proc. Path. Soc., Philadelphia, 1914, **16**, 67.
79. Kline, B. S.: Jour. Exper. Med., 1917, **26**, 239.
80. Hess, J. H.: Arch. Pediat., 1917, **39**, 686.
81. Letulle, M.: Presse méd., 1917, **25**, 288.
82. Barrgar: Canada Med. Assn. Jour., 1917, **8**, 666.
83. Haythorn, S. R.: Internat. Assn. Med. Mus. Bull., 1918, No. 7, p. 49.
84. Wang, S. L.: Med. Rec., 1918, **93**, 590.

OBSERVATIONS ON THE CURABILITY OF GASTRIC ULCER, WITH A REPORT OF FOURTEEN CASES OF HEALED LESSER CURVATURE ULCERS.[1]

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Gastric ulcer of the lesser curvature type when subjected to medical treatment affords a good opportunity for observation during the period of healing and thereafter. Medical literature is as yet meager as to the number of such observations and the possibilities of medical cures. I deem it therefore worth while to report a series of 14 cases of gastric ulcer of the lesser curvature type presenting a niche anywhere between the two incisuras, either overriding the lesser curvature or close to it. All these have been subjected to medical treatment and have been observed for periods ranging anywhere up to four and a half years. Up to the present time all these ulcers have remained healed. This statement is based not only upon the subjective clinical evidence of the improvement and well-being of these patients, but upon definite objective data as recorded from time to time on roentgen plates, where not only a disappearance of the ulcer crater is noted, but also a restoration of

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